Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report #88: Friday, 04 March 2022

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. Please reach out with questions, suggestions for future topics, or any other feedback. If this report made a difference or impacted patient care, please let me know!

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the list of retracted papers from Retraction Watch.

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The Big Picture

News in Brief

"The White House has a new plan for COVID-19 aimed at getting things back to normal" (NPR; see also: National COVID-19 Preparedness Plan).

"The pandemic: a series of failures, a few miracles — and a lesson for next time, global health experts say" (STAT).

"More than 140 million Americans, or about 43% of the country, have had COVID-19, according to the CDC's updated estimates of antibody seroprevalence" (Medpage; see also: CDC's COVID Data Tracker).

"Most Americans say the coronavirus is not yet under control and support restrictions to try to manage it, Post-ABC poll finds" (WP).

"Commit to transparent COVID data until the WHO declares the pandemic is over" (Nature).

"The pandemic pummeled long-term care – it may not recover quickly, experts warn" (NPR).

"Are we ready for COVID-19 as a central theme in literature?" (NPR)

Journal Articles

JAMA Netw Open: Successfully Implementing Digital Health to Ensure Future Global Health Security During Pandemics: A Consensus Statement (23 February 2022)

> "Question: What digital health recommendations should be adopted by the global health community to address the challenges of current and future pandemics?
>
> Findings: By engaging a diverse stakeholder group of 13 leaders in the fields of public health, digital health, and health care, a consensus was reached on how to implement digital health recommendations to address the challenges of current and future pandemics across 5 main themes: team, transparency and trust, technology, techquity (the strategic development and deployment of technology in health care and health to achieve health equity), and transformation.
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> Meaning: This consensus statement provides a roadmap for the implementation of digital health policy by stakeholders, including governments, to prepare for and address current and future pandemics."
>
> See also: commentary

Ann Intern Med: Contribution of Individual- and Neighborhood-Level Social, Demographic, and Health Factors to COVID-19 Hospitalization Outcomes (22 February 2022)

"Background: Although disparities in COVID-19 outcomes have been observed, factors contributing to these differences are not well understood.

Objective: To determine whether COVID-19 hospitalization outcomes are related to neighborhood-level social vulnerability, independent of patient-level clinical factors.

Design: Pooled cross-sectional study of prospectively collected data.

Setting: 38 Michigan hospitals.

Patients: Adults older than 18 years hospitalized for COVID-19 in a participating site between March and December 2020.

Measurements: COVID-19 outcomes included acute organ dysfunction, organ failure, invasive mechanical ventilation, intensive care unit stay, death, and discharge disposition. Social vulnerability was measured by the social vulnerability index (SVI), a composite measure of social disadvantage.

Results: Compared with patients in low-vulnerability ZIP codes, those living in high-vulnerability ZIP codes were more frequently treated in the intensive care unit (29.0% vs. 24.5%); more frequently received mechanical ventilation (19.3% vs. 14.2%); and experienced higher rates of organ dysfunction (51.9% vs. 48.6%), organ failure (54.7% vs. 51.6%), and in-hospital death (19.4% vs. 16.7%). In mixed-effects regression analyses accounting for age, sex, and comorbid conditions, an increase in a patient's neighborhood SVI by 0.25 (1 quartile) was associated with greater likelihood of mechanical ventilation (increase of 2.1 percentage points), acute organ dysfunction (increase of 2.8 percentage points), and acute organ failure (increase of 2.8 percentage points) but was not associated with intensive care unit stay, mortality, or discharge disposition.

Limitation: Observational data focused on hospitalizations in a single state.

Conclusion: Hospitalized patients with COVID-19 from socially vulnerable neighborhoods presented with greater illness severity and required more intensive treatment, but once hospitalized they did not experience differences in hospital mortality or discharge disposition. Policies that target socially vulnerable neighborhoods and access to COVID-19 care may help ameliorate health disparities."

SARS-CoV-2 Virus and Variants

News in Brief

"Why does the Omicron sub-variant spread faster than the original? Early studies suggest that the BA.2 lineage might prolong the Omicron wave, but won't necessarily cause a fresh surge of COVID infections" (Nature).

"Omicron's lasting mysteries: four questions scientists are racing to answer" (Nature).

"The next variant: three key questions about what's after Omicron (Nature).

"An investigation led by Canadian Food Inspection Agency scientists has identified a new and highly divergent lineage of SARS-CoV-2, the virus that causes COVID-19 in white-tailed deer in that country" (CIDRAP; see also: bioRxiv preprint).

"Wuhan market was epicentre of pandemic's start, studies suggest: Report authors say that the coronavirus SARS-CoV-2 jumped from animals sold at the market into people twice in late 2019 — but some scientists want more definitive evidence" (Nature).

Journal Articles

NEJM: Population Immunity and Covid-19 Severity with Omicron Variant in South Africa (23 February 2022)

> "Background: The B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified on November 25, 2021, in Gauteng province, South Africa. Data regarding the seroprevalence of SARS-CoV-2 IgG in Gauteng before the fourth wave of coronavirus disease 2019 (Covid-19), in which the omicron variant was dominant, are needed.
>
> Methods: We conducted a seroepidemiologic survey from October 22 to December 9, 2021, in Gauteng to determine the seroprevalence of SARS-CoV-2 IgG. Households included in a previous seroepidemiologic survey (conducted from November 2020 to January 2021) were contacted; to account for changes in the survey population, there was a 10% increase in the households contacted, with the use of the same sampling framework. Dried-blood-spot samples were tested for IgG against SARS-CoV-2 spike protein and nucleocapsid protein with the use of quantitative assays. We also evaluated Covid-19 epidemiologic trends in Gauteng, including cases, hospitalizations, recorded deaths, and excess deaths from the start of the pandemic through January 12, 2022.
>
> Results: Samples were obtained from 7010 participants, of whom 1319 (18.8%) had received a Covid-19 vaccine. The seroprevalence of SARS-CoV-2 IgG ranged from 56.2% (95% confidence interval [CI], 52.6 to 59.7) among children younger than 12 years of age to

79.7% (95% CI, 77.6 to 81.5) among adults older than 50 years of age. Vaccinated participants were more likely to be seropositive for SARS-CoV-2 than unvaccinated participants (93.1% vs. 68.4%). Epidemiologic data showed that the incidence of SARS-CoV-2 infection increased and subsequently declined more rapidly during the fourth wave than it had during the three previous waves. The incidence of infection was decoupled from the incidences of hospitalization, recorded death, and excess death during the fourth wave, as compared with the proportions seen during previous waves.

Conclusions: Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng before the omicron-dominant wave of Covid-19. Epidemiologic data showed a decoupling of hospitalizations and deaths from infections while omicron was circulating."

Transmission, Exposure, and Testing

News in Brief

"As mask mandates fade, experts say use of masks likely will not" (STAT).

"It's safe to unmask in many places, says the CDC. These experts aren't quite ready" (NPR; see also: CDC community level data).

Journal Articles

MMWR: SARS-CoV-2 B.1.1.529 (Omicron) Variant Transmission Within Households — Four U.S. Jurisdictions, November 2021–February 2022 (04 March 2022)

"What is already known about this topic? The SARS-CoV-2 B.1.1.529 (Omicron) variant contributed to a surge of SARS-CoV-2 infections in the United States during December 2021–January 2022.

What is added by this report? In a study of household transmission in four U.S. jurisdictions, Omicron infection resulted in high transmission among household contacts, particularly among those who lived with index patients who were not vaccinated or who did not take measures to reduce the risk of transmission to household contacts.

What are the implications for public health practice? Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are important to reduce Omicron transmission in household settings."

Clin Infect Dis: Airborne SARS-CoV-2 in hospitals – effects of aerosol-generating procedures, HEPA-filtration units, patient viral load and physical distance (28 February 2022)

> "Background: Transmission of covid-19 can occur through inhalation of fine droplets or aerosols containing infectious virus. The objective of this study was to identify situations, patient characteristics, environmental parameters and aerosol-generating procedures (AGPs) associated with airborne SARS-CoV-2 virus.
>
> Methods: Air samples were collected near hospitalised covid-19 patients and analysed by RT-qPCR. Results were related to distance to the patient, most recent patient diagnostic PCR Ct-value, room ventilation and ongoing potential AGP.
>
> Results: In total 310 air samples were collected, and of these 26 (8%) were positive. Of the 231 samples from patient rooms, 22 (10%) were positive for SARS-CoV-2. Positive air samples were associated with a low patient Ct-value (OR 5.0 for a Ct-value <25 vs >25, p=0.01, 95% confidence interval 1.18 to 29.5) and a shorter physical distance to the patient (OR 2.0 for every meter closer to the patient, p=0.05, CI 1.0 to 3.8). A mobile HEPA-filtration unit in the room decreased the proportion of positive samples (OR 0.3, p=0.02, CI 0.12 to 0.98). No association was observed between SARS-CoV-2 positive air samples and mechanical ventilation, high flow nasal cannula, nebulizer treatment or non-invasive ventilation. An association was found with positive expiratory pressure (PEP) training (p<0.01) and a trend towards association for airway manipulation, including bronchoscopies and in- and extubations.
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> Conclusions: Our results show that major risk factors for airborne SARS-CoV-2 include short physical distance, high patient viral load and poor room ventilation. AGPs, as traditionally defined, seem to be of secondary importance."

MMWR: Results from a Test-to-Release from Isolation Strategy Among Fully Vaccinated National Football League Players and Staff Members with COVID-19 — United States, December 14–19, 2021 (25 February 2022)

> "What is already known about this topic? On December 16, 2021, the National Football League (NFL) updated its test-to-release from COVID-19 isolation protocols in response to increasing COVID-19 cases and predominance of the SARS-CoV-2 Omicron variant.
>
> What is added by this report? Among 173 vaccinated adults with COVID-19 undergoing serial reverse transcription–polymerase chain reaction (RT-PCR) testing during Omicron predominance, 46% received a negative or high cycle threshold RT-PCR test result on or before day 6 postdiagnosis.
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> What are the implications for public health practice? Although a positive RT-PCR test result does not necessarily indicate infectiousness, these data indicate that persons with COVID-

19 should continue to take precautions, including correct and consistent mask use, for a full 10 days after symptom onset or after initial positive test result if they are asymptomatic."

MMWR: Antigen Test Positivity After COVID-19 Isolation — Yukon-Kuskokwim Delta Region, Alaska, January–February 2022 (25 February 2022)

"What is already known about this topic? Positive rapid antigen test results after SARS-CoV-2 infection have been associated with the presence of viable virus, but the role of antigen tests in isolation guidance for persons with SARS-CoV-2 infection is unclear.

What is added by this report? Between 5 and 9 days after symptom onset or after initial diagnosis with SARS-CoV-2 infection, 54% of persons had positive SARS-CoV-2 antigen test results. The proportion of positive results declined over time. Negative follow-up antigen test results were associated with asymptomatic infection, previous infection, and being vaccinated.

What are the implications for public health practice? Antigen tests might be a useful tool to guide recommendations for isolation after SARS-CoV-2 infection."

BMJ: SARS-CoV-2 antigen lateral flow tests for detecting infectious people: linked data analysis (23 February 2022)

"Objectives: To investigate the proportion of lateral flow tests (LFTs) that produce negative results in those with a high risk of infectiousness from SARS-CoV-2, to investigate the impact of the stage and severity of disease, and to compare predictions made by influential mathematical models with findings of empirical studies.

Design: Linked data analysis combining empirical evidence of the accuracy of the Innova LFT, the probability of positive viral culture or transmission to secondary cases, and the distribution of viral loads of SARS-CoV-2 in individuals in different settings.

Setting: Testing of individuals with symptoms attending NHS Test-and-Trace centres across the UK, residents without symptoms attending municipal mass testing centres in Liverpool, and students without symptoms screened at the University of Birmingham.

Participants: Evidence for the sensitivity of the Innova LFT, based on 70 individuals with SARS-CoV-2 and LFT results. Infectiousness was based on viral culture rates on 246 samples (176 people with SARS-CoV-2) and secondary cases among 2 474 066 contacts; distributions of cycle threshold (Ct) values from 231 497 index individuals attending NHS Test-and-Trace centres; 70 people with SARS-CoV-2 detected in Liverpool and 62 people with SARS-CoV-2 in Birmingham (54 imputed).

Main outcome measures: The predicted proportions who were missed by LFT and viral culture positive and missed by LFT and sources of secondary cases, in each of the three settings. Predictions were compared with those made by mathematical models.

> Results: The analysis predicted that of those with a viral culture positive result, Innova would miss 20% attending an NHS Test-and-Trace centre, 29% without symptoms attending municipal mass testing, and 81% attending university screen testing without symptoms, along with 38%, 47%, and 90% of sources of secondary cases. In comparison, two mathematical models underestimated the numbers of missed infectious individuals (8%, 10%, and 32% in the three settings for one model, whereas the assumptions from the second model made it impossible to miss an infectious individual). Owing to the paucity of usable data, the inputs to the analyses are from limited sources.
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> Conclusions: The proportion of infectious people with SARS-CoV-2 missed by LFTs is substantial enough to be of clinical importance. The proportion missed varied between settings because of different viral load distributions and is likely to be highest in those without symptoms. Key models have substantially overestimated the sensitivity of LFTs compared with empirical data. An urgent need exists for additional robust well designed and reported empirical studies from intended use settings to inform evidence based policy."

MMWR: Notes from the Field: Outbreak of COVID-19 Among a Highly Vaccinated Population Aboard a U.S. Navy Ship After a Port Visit — Reykjavik, Iceland, July 2021 (18 February 2022)

> "This outbreak in the enclosed environment of a ship suggests that high vaccination rates, in combination with COVID-19 prevention measures, can substantially reduce the spread of SARS-CoV-2, despite the high transmissibility of the Delta variant and introduction of SARS-CoV-2 into a congregate setting. Infections among vaccinated persons did occur, which is expected, but symptoms were mild. Vaccination, in coordination with multicomponent prevention strategies, are critical to limiting SARS-CoV-2 transmission and COVID-19–related illness."

J Infect: High amounts of SARS-CoV-2 in aerosols exhaled by patients with Omicron variant infection (17 February 2022)

> Letter to the editor; highlights: "At the early (1-5 days) and middle (6-10 days) stages after the onset of COVID-19 symptom, Omicron variant patients exhaled ten million virus particles per hour. In the late stage (11-19 days), the breath emission rate was still as high as those of the two other stages. Omicron variant may be highly transmissible."

PLoS One: Identifying SARS-COV-2 infected patients through canine olfactive detection on axillary sweat samples; study of observed sensitivities and specificities within a group of trained dogs (14 February 2022)

> "There is an increasing need for rapid, reliable, non-invasive, and inexpensive mass testing methods as the global COVID-19 pandemic continues. Detection dogs could be a possible solution to identify individuals infected with SARS-CoV-2. Previous studies have shown that dogs can detect SARS-CoV-2 on sweat samples. This study aims to establish the dogs'

sensitivity (true positive rate) which measures the proportion of people with COVID-19 that are correctly identified, and specificity (true negative rate) which measures the proportion of people without COVID-19 that are correctly identified. Seven search and rescue dogs were tested using a total of 218 axillary sweat samples (62 positive and 156 negative) in olfaction cones following a randomised and double-blind protocol. Sensitivity ranged from 87% to 94%, and specificity ranged from 78% to 92%, with four dogs over 90%. These results were used to calculate the positive predictive value and negative predictive value for each dog for different infection probabilities (how likely it is for an individual to be SARS-CoV-2 positive), ranging from 10–50%. These results were compared with a reference diagnostic tool which has 95% specificity and sensitivity. Negative predictive values for six dogs ranged from ≥98% at 10% infection probability to ≥88% at 50% infection probability compared with the reference tool which ranged from 99% to 95%. Positive predictive values ranged from ≥40% at 10% infection probability to ≥80% at 50% infection probability compared with the reference tool which ranged from 68% to 95%. This study confirms previous results, suggesting that dogs could play an important role in mass-testing situations. Future challenges include optimal training methods and standardisation for large numbers of detection dogs and infrastructure supporting their deployment."

COVID-19 Vaccines

News in Brief

"COVID-19: talk of 'vaccine hesitancy' lets governments off the hook" (Nature).

"Fourth dose of COVID vaccine offers only slight boost against Omicron infection" (Nature).

Journal Articles

JAMA Otolaryngol Head Neck Surg: Association Between the BNT162b2 Messenger RNA COVID-19 Vaccine and the Risk of Sudden Sensorineural Hearing Loss (24 February 2022)

"Question: Is there an association between the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine and sudden sensorineural hearing loss (SSNHL)?

Findings: In this cohort study of 2 602 557 patients in Israel, an association was found between the BNT162b2 mRNA COVID-19 vaccine and SSNHL as reflected by the high ratio of observed to expected SSNHL cases; however, the effect size was very small.

Meaning: Considering the small effect size of this association and the good prognosis for patients with SSNHL, the potential influence of this condition on public health appears to be relatively minor."

JAMA Otolaryngol Head Neck Surg: Assessment of Sudden Sensorineural Hearing Loss After COVID-19 Vaccination (24 February 2022)

"Question: Is COVID-19 vaccination associated with sudden sensorineural hearing loss (SSNHL)?

Findings: In this cross-sectional study and case series involving 555 cases of SSNHL among adults reported to the Centers for Disease Control and Prevention Vaccine Adverse Events Reporting System, no increase in the rate of hearing loss after COVID-19 vaccination was found compared with the incidence in the general population. Assessment of 21 adult patients who presented to tertiary care centers with SSNHL after COVID-19 vaccination did not reveal any apparent associations with respect to clinical or demographic factors.

Meaning: These results suggest that there is no association between vaccination and the development of SSNHL among adults who received a COVID-19 vaccine."

PLoS Med: Association of COVID-19 vaccines ChAdOx1 and BNT162b2 with major venous, arterial, or thrombocytopenic events: A population-based cohort study of 46 million adults in England (22 February 2022)

"Background: Thromboses in unusual locations after the Coronavirus Disease 2019 (COVID-19) vaccine ChAdOx1-S have been reported, although their frequency with vaccines of different types is uncertain at a population level. The aim of this study was to estimate the population-level risks of hospitalised thrombocytopenia and major arterial and venous thromboses after COVID-19 vaccination.

Methods and findings: In this whole-population cohort study, we analysed linked electronic health records from adults living in England, from 8 December 2020 to 18 March 2021. We estimated incidence rates and hazard ratios (HRs) for major arterial, venous, and thrombocytopenic outcomes 1 to 28 and >28 days after first vaccination dose for ChAdOx1-S and BNT162b2 vaccines. Analyses were performed separately for ages <70 and ≥70 years and adjusted for age, age2, sex, ethnicity, and deprivation. We also prespecified adjustment for anticoagulant medication, combined oral contraceptive medication, hormone replacement therapy medication, history of pulmonary embolism or deep vein thrombosis, and history of coronavirus infection in analyses of venous thrombosis; and diabetes, hypertension, smoking, antiplatelet medication, blood pressure lowering medication, lipid lowering medication, anticoagulant medication, history of stroke, and history of myocardial infarction in analyses of arterial thromboses. We selected further covariates with backward selection. Of 46 million adults, 23 million (51%) were women; 39 million (84%) were <70;

and 3.7 million (8.1%) Asian or Asian British, 1.6 million (3.5%) Black or Black British, 36 million (79%) White, 0.7 million (1.5%) mixed ethnicity, and 1.5 million (3.2%) were of another ethnicity. Approximately 21 million (46%) adults had their first vaccination between 8 December 2020 and 18 March 2021. The crude incidence rates (per 100,000 person-years) of all venous events were as follows: prevaccination, 140 [95% confidence interval (CI): 138 to 142]; ≤28 days post-ChAdOx1-S, 294 (281 to 307); >28 days post-ChAdOx1-S, 359 (338 to 382), ≤28 days post-BNT162b2-S, 241 (229 to 253); >28 days post-BNT162b2-S 277 (263 to 291). The crude incidence rates (per 100,000 person-years) of all arterial events were as follows: prevaccination, 546 (95% CI: 541 to 555); ≤28 days post-ChAdOx1-S, 1,211 (1,185 to 1,237); >28 days post-ChAdOx1-S, 1678 (1,630 to 1,726), ≤28 days post-BNT162b2-S, 1,242 (1,214 to 1,269); >28 days post-BNT162b2-S, 1,539 (1,507 to 1,572). Adjusted HRs (aHRs) 1 to 28 days after ChAdOx1-S, compared with unvaccinated rates, at ages <70 and ≥70 years, respectively, were 0.97 (95% CI: 0.90 to 1.05) and 0.58 (0.53 to 0.63) for venous thromboses, and 0.90 (0.86 to 0.95) and 0.76 (0.73 to 0.79) for arterial thromboses. Corresponding aHRs for BNT162b2 were 0.81 (0.74 to 0.88) and 0.57 (0.53 to 0.62) for venous thromboses, and 0.94 (0.90 to 0.99) and 0.72 (0.70 to 0.75) for arterial thromboses. aHRs for thrombotic events were higher at younger ages for venous thromboses after ChAdOx1-S, and for arterial thromboses after both vaccines. Rates of intracranial venous thrombosis (ICVT) and of thrombocytopenia in adults aged <70 years were higher 1 to 28 days after ChAdOx1-S (aHRs 2.27, 95% CI: 1.33 to 3.88 and 1.71, 1.35 to 2.16, respectively), but not after BNT162b2 (0.59, 0.24 to 1.45 and 1.00, 0.75 to 1.34) compared with unvaccinated. The corresponding absolute excess risks of ICVT 1 to 28 days after ChAdOx1-S were 0.9 to 3 per million, varying by age and sex. The main limitations of the study are as follows: (i) it relies on the accuracy of coded healthcare data to identify exposures, covariates, and outcomes; (ii) the use of primary reason for hospital admission to measure outcome, which improves the positive predictive value but may lead to an underestimation of incidence; and (iii) potential unmeasured confounding.

Conclusions: In this study, we observed increases in rates of ICVT and thrombocytopenia after ChAdOx1-S vaccination in adults aged <70 years that were small compared with its effect in reducing COVID-19 morbidity and mortality, although more precise estimates for adults aged <40 years are needed. For people aged ≥70 years, rates of arterial or venous thrombotic events were generally lower after either vaccine compared with unvaccinated, suggesting that either vaccine is suitable in this age group."

PLoS Med: First dose ChAdOx1 and BNT162b2 COVID-19 vaccinations and cerebral venous sinus thrombosis: A pooled self-controlled case series study of 11.6 million individuals in England, Scotland, and Wales (22 February 2022)

"Background: Several countries restricted the administration of ChAdOx1 to older age groups in 2021 over safety concerns following case reports and observed versus expected

analyses suggesting a possible association with cerebral venous sinus thrombosis (CVST). Large datasets are required to precisely estimate the association between Coronavirus Disease 2019 (COVID-19) vaccination and CVST due to the extreme rarity of this event. We aimed to accomplish this by combining national data from England, Scotland, and Wales.

Methods and findings: We created data platforms consisting of linked primary care, secondary care, mortality, and virological testing data in each of England, Scotland, and Wales, with a combined cohort of 11,637,157 people and 6,808,293 person years of follow-up. The cohort start date was December 8, 2020, and the end date was June 30, 2021. The outcome measure we examined was incident CVST events recorded in either primary or secondary care records. We carried out a self-controlled case series (SCCS) analysis of this outcome following first dose vaccination with ChAdOx1 and BNT162b2. The observation period consisted of an initial 90-day reference period, followed by a 2-week prerisk period directly prior to vaccination, and a 4-week risk period following vaccination. Counts of CVST cases from each country were tallied, then expanded into a full dataset with 1 row for each individual and observation time period. There was a combined total of 201 incident CVST events in the cohorts (29.5 per million person years). There were 81 CVST events in the observation period among those who a received first dose of ChAdOx1 (approximately 16.34 per million doses) and 40 for those who received a first dose of BNT162b2 (approximately 12.60 per million doses). We fitted conditional Poisson models to estimate incidence rate ratios (IRRs). Vaccination with ChAdOx1 was associated with an elevated risk of incident CVST events in the 28 days following vaccination, IRR = 1.93 (95% confidence interval (CI) 1.20 to 3.11). We did not find an association between BNT162b2 and CVST in the 28 days following vaccination, IRR = 0.78 (95% CI 0.34 to 1.77). Our study had some limitations. The SCCS study design implicitly controls for variables that are constant over the observation period, but also assumes that outcome events are independent of exposure. This assumption may not be satisfied in the case of CVST, firstly because it is a serious adverse event, and secondly because the vaccination programme in the United Kingdom prioritised the clinically extremely vulnerable and those with underlying health conditions, which may have caused a selection effect for individuals more prone to CVST. Although we pooled data from several large datasets, there was still a low number of events, which may have caused imprecision in our estimates.

Conclusions: In this study, we observed a small elevated risk of CVST events following vaccination with ChAdOx1, but not BNT162b2. Our analysis pooled information from large datasets from England, Scotland, and Wales. This evidence may be useful in risk-benefit analyses of vaccine policies and in providing quantification of risks associated with vaccination to the general public."

Nat Med: Effectiveness of mRNA-1273 against SARS-CoV-2 Omicron and Delta variants (21 February 2022)

> "SARS-CoV-2 Omicron (B.1.1.529) variant is highly transmissible with potential immune escape. We conducted a test-negative case-control study to evaluate mRNA-1273 vaccine effectiveness (VE) against infection and hospitalization with Omicron or Delta. The large, diverse study population included 26,683 SARS-CoV-2 test-positive cases with variants determined by S-gene target failure status (16% Delta, 84% Omicron). The 2-dose VE against Omicron infection at 14-90 days was 44.0% (95% CI, 35.1-51.6%) but declined quickly. The 3-dose VE was 93.7% (92.2-94.9%) and 86.0% (78.1-91.1%) against Delta infection and 71.6% (69.7-73.4%) and 47.4% (40.5-53.5%) against Omicron infection at 14-60 days and >60 days, respectively. The 3-dose VE was 29.4% (0.3-50.0%) against Omicron infection in immunocompromised individuals. The 3-dose VE against hospitalization with Delta or Omicron was >99% across the entire study population. Our findings demonstrate high, durable 3-dose VE against Delta infection but lower effectiveness against Omicron infection, particularly among immunocompromised people. However, 3-dose VE of mRNA-1273 was high against hospitalization with Delta and Omicron variants."

J Med Virol: Vaccination provides protection from respiratory deterioration and death among hospitalized COVID-19 patients: Differences between vector and mRNA vaccines (20 February 2022)

> "Outcomes of 109 hospitalized COVID-19 patients who received at least one vaccine dose 14 or more days prior the disease onset were retrospectively compared to control cohort of 109 age, sex, and Charlson comorbidity index-matched patients chosen among 2990 total hospitalized patients in our tertiary-level institution in a period from January to June 2021. Among 109 vaccinated patients, 84 patients were partially and 25 fully vaccinated. Vaccinated patients experienced significantly lower 30 days mortality (30% vs. 49%; hazard ratio [HR]: 0.56 [0.37-0.85]; p = 0.008), less frequently required high flow oxygen therapy (17% vs. 34%; HR: 0.45 [0.26-0.76]; p = 0.005), and mechanical ventilation (8% vs. 18%; HR: 0.41 [0.20-0.88]; p = 0.027) in comparison to the matched cohort of unvaccinated patients. More favorable survival was observed in patients receiving vector in comparison to messenger RNA (mRNA) vaccine types in unadjusted analysis (30 days mortality 18% vs. 40%; HR: 0.45 [0.25-0.79]; p = 0.034). In the multivariable Cox regression analysis model both mRNA (HR: 0.59 [0.36-0.98]; p = 0.041) and vector vaccine types (HR: 0.30 [0.15-0.60]; p < 0.001) were associated with improved survival in comparison to unvaccinated patients, independently of age (HR: 1.03 [1.01-1.06]; p = 0.011), male sex (HR: 1.78 [1.14-2.76]; p = 0.010), severity of illness (HR: 2.06 [1.36-3.10]; p < 0.001) and functional status on admission (HR: 1.42 [1.07-1.85]; p = 0.013)."

Breakthrough Infections and Reinfections

News in Brief

"Infection with the SARS-CoV-2 Omicron BA.2 subvariant shortly after an initial infection with the Omicron BA.1 subvariant—the original Omicron strain—is rare, occurring mostly in young, unvaccinated people with mild symptoms, according to a non–peer-reviewed Danish study" (CIDRAP; see also: medRxiv preprint).

Journal Articles

Clin Case Rep: Confirmed reinfection with SARS-CoV-2 during a pregnancy: A case report (15 February 2022)

> "Pregnancy might impact immunity after SARS-CoV-2 infection and/or vaccination. We describe the first case of reinfection with SARS-CoV-2 during a pregnancy. While the mother lacked detectable antibodies 2 months after the first infection, both mother and baby had IgG antibodies at delivery. Infection did not cause any adverse pregnancy outcome."

Emerg Infect Dis: COVID-19 Vaccination Coverage, Behaviors, and Intentions among Adults with Previous Diagnosis, United States (03 February 2022)

> "To determine the extent of gaps in coronavirus disease (COVID-19) vaccine coverage among those in the United States with and without previous COVID-19 diagnoses, we used July 21–August 2, 2021, data from a large, nationally representative survey (Household Pulse Survey).
>
> We analyzed vaccine receipt (≥1 dose and full vaccination) and intention to be vaccinated for 63,266 persons. Vaccination receipt was lower among those who had a prior diagnosis of COVID-19 compared to those without: >1 dose: 73% and 85%, respectively, p<0.001; full vaccination: 69% and 82%, respectively, p<0.001). Reluctance to be vaccinated was higher among those with a previous COVID-19 diagnosis (14%) than among those without (9%). These findings suggest the need to focus educational and confidence-building interventions on adults when they receive a COVID-19 diagnosis, during clinic visits, or at the time of discharge if hospitalized and to better educate the public about the value of being vaccinated, regardless of previous COVID-19 status."

Treatments and Management

News in Brief

IDSA has updated its COVID-19 guidelines with 2 new recommendations for using lopinavir/ritonavir as prophylaxis (IDSA).

Updated NIH COVID-19 treatment guidelines support the use of the monoclonal antibody bebtelovimab for the treatment of high-risk outpatients, though it landed as an alternative behind nirmatrelvir-ritonavir, sotrovimab, and remdesivir (NIH).

"Doctors find limited use for less effective COVID pill" (NPR).

Long Reads

"Hundreds of COVID trials could provide a deluge of new drugs. Two years into the pandemic, the COVID-19 drugs pipeline is primed to pump out novel treatments — and fresh uses for familiar therapies" (Nature).

Journal Articles

JAMA Netw Open: Comparison of Outcomes and Process of Care for Patients Treated at Hospitals Dedicated for COVID-19 Care vs Other Hospitals (03 March 2022)

> "Question: Is treatment of COVID-19 at a dedicated hospital associated with improved care processes and outcomes?
>
> Findings: In this cohort study of 5504 patients with COVID-19, lower mortality rates were found in dedicated COVID-19 hospitals vs other hospitals.
>
> Meaning: Results of this study suggest that treatment at dedicated COVID-19 hospitals may be associated with reducing in-hospital mortality; this model may be useful during future pandemics."

JAMA Netw Open: Association of COVID-19 Infection With Survival After In-Hospital Cardiac Arrest Among US Adults (02 March 2022)

> "This cohort study examines the association of COVID-19 infection with survival outcomes of US adults after in-hospital cardiac arrest….
>
> In this cohort study, approximately 1 in 4 patients with IHCA identified in the GWTG-R registry during 2020 had a suspected or confirmed COVID-19 infection. This observation underscores the sizable effect of the pandemic on in-hospital resuscitation. Even after accounting for substantial differences between patients with and without COVID-19 infection, the disease was associated with a one-third lower rate of overall survival and was

accompanied by a 30% increased rate of delayed defibrillation in shockable IHCA. Although delays in resuscitation, especially defibrillation, may have contributed to lower survival, the negative association of COVID-19 with survival in this study was consistent across subgroups, including patients who received timely treatment with defibrillation and epinephrine."

Clin Infect Dis: Sarilumab-COVID-19 Study Team. Efficacy and Safety of Sarilumab in Hospitalized Patients With COVID-19: A Randomized Clinical Trial (26 February 2022)

"Background: Open-label platform trials and a prospective meta-analysis suggest efficacy of anti-IL-6R therapies in hospitalized patients with COVID-19 receiving corticosteroids. This study evaluated the efficacy and safety of sarilumab, an anti-IL-6R monoclonal antibody, in the treatment of hospitalized patients with COVID-19.

Methods: In this adaptive, phase 2/3, randomized, double-blind, placebo-controlled trial, adults hospitalized with COVID-19 (ClinicalTrials.gov: NCT04315298) received intravenous sarilumab or placebo. The phase 3 primary analysis population included patients with critical COVID-19 receiving mechanical ventilation randomized to sarilumab 400 mg or placebo. The primary outcome was proportion of patients with ≥1-point improvement in clinical status from baseline to day 22.

Results: There were 457 and 1365 patients randomized and treated in phases 2 and 3, respectively. In phase 3, patients with critical COVID-19 receiving mechanical ventilation (n = 298; 28.2% on corticosteroids), the proportion with ≥1-point improvement in clinical status (alive, not receiving mechanical ventilation) at day 22 was 43.2% in sarilumab and 35.5% in placebo (risk difference +7.5%; 95% CI, -7.4 to 21.3; P = .3261), a relative risk improvement of 21.7%. In post-hoc analyses pooling phase 2 and 3 critical patients receiving mechanical ventilation, the hazard ratio for death in sarilumab versus placebo was 0.76 (95% CI, .51-1.13) overall and 0.49 (95% CI, .25-.94) in patients receiving corticosteroids at baseline.

Conclusions: This study did not establish the efficacy of sarilumab in hospitalized patients with severe/critical COVID-19. Post-hoc analyses were consistent with other studies that found a benefit of sarilumab in patients receiving corticosteroids."

Am J Respir Crit Care Med: Association Between Availability of ECMO and Mortality in COVID-19 Patients Eligible for ECMO: A Natural Experiment (24 February 2022)

Summary taken from CIDRAP: "Vanderbilt University researchers prospectively analyzed data from all COVID-19 patients referred to a single center for ECMO from Jan 1 to Aug 31, 2021. Patients qualified for ECMO if they were younger than 60 years, had a body mass index (BMI) less than 55 kg/m2, had received mechanical ventilation for more than 7 days,

> or had irreversible neurologic injury, chronic lung disease, cancer, or advanced multi-organ dysfunction….
>
> A systematic assessment of the health system's resources to provide ECMO for eligible patients (ie, equipment, personnel, and intensive care unit bed availability) was conducted. If resources were available, patients were started on ECMO and then transferred to an ECMO center, but patients were not referred if resources were already at capacity. Patients transferred to other regional ECMO centers were started on the treatment after arrival at the ECMO facility….
>
> Among 240 COVID-19 patients referred for ECMO, 26 (10.8%) didn't complete the referral evaluation, 44 (18.3%) didn't meet the criteria for severity of lung injury, 80 (33.3%) had contraindications to treatment, and 90 (37.5%) were eligible for ECMO. Median patient age was 40 years, and 27.8% were female.
>
> Fifty-five patients (61.1%) were not transferred to an ECMO facility and didn't receive the therapy because of a shortage of resources. Forty-nine of these patients (89.1%) died in the hospital, versus 15 of 35 patients (42.9%) who received ECMO (adjusted hazard ratio, 0.23; 95% confidence interval, 0.12 to 0.43).
>
> The health system had ECMO capacity for 35 patients (38.9%), of whom 24 were started on the treatment at the hospital before transfer to an ECMO facility, while 11 were transferred to another regional center. Eight of the 11 patients were started on treatment after arrival at the center, and 3 died or developed a contraindication to ECMO after arrival but before treatment was started. Characteristics of both groups of patients were similar at the time of referral."

Ann Thorac Surg: Multi-institutional Analysis of 505 COVID-19 Patients Supported with ECMO: Predictors of Survival (18 February 2022)

> "Background: We reviewed our experience with 505 patients with confirmed COVID-19 supported with ECMO at 45 hospitals and estimated risk factors for mortality.
>
> Methods: A multi-institutional database was created and utilized to assess all patients with COVID-19 who were supported with ECMO. A Bayesian mixed-effects logistic regression model was estimated to assess the effect on survival of days between COVID-19 diagnosis and intubation, as well as age at ECMO cannulation.
>
> Results: Median time on ECMO was 18 days (interquartile range=10-29). All 505 patients have separated from ECMO: 194 patients (38.4%) survived and 311 patients (61.6%) died. Survival with veno-venous ECMO was 184 of 466 patients (39.5%), while survival with veno-arterial ECMO was 8 of 30 patients (26.7%). Survivors had lower median age (44 versus 51 years, $p<0.001$) and shorter median time interval from diagnosis to intubation (7 days versus 11 days, $p=0.001$). Adjusting for several confounding factors, we estimated that an

ECMO patient intubated on day 14 post COVID-19 diagnosis vs day 4 had a relative odds of survival of 0.65 (95% Credible Interval [CrI]:0.44-0.96, posterior probability of negative effect: 98.5%). Age was also negatively associated with survival: relative to a 38-year-old we estimated that a 57-year-old patient had a relative odds of survival of 0.43 (95% CrI:0.30-0.61, posterior probability of negative effect: >99.99%).

Conclusions: ECMO facilitates salvage and survival of select critically ill patients with COVID-19. Survivors tend to be younger and have shorter time from diagnosis to intubation. Survival of patients supported with only veno-venous ECMO was 39.5%."

Sci Rep: Convalescent plasma in the treatment of moderate to severe COVID-19 pneumonia: a randomized controlled trial (PROTECT-Patient Trial) (15 February 2022)

"There is a need for effective therapy for COVID-19 pneumonia. Convalescent plasma has antiviral activity and early observational studies suggested benefit in reducing COVID-19 severity. We investigated the safety and efficacy of convalescent plasma in hospitalized patients with COVID-19 in a population with a high HIV prevalence and where few therapeutic options were available.

We performed a double-blinded, multicenter, randomized controlled trial in one private and three public sector hospitals in South Africa. Adult participants with COVID-19 pneumonia requiring non-invasive oxygen were randomized 1:1 to receive a single transfusion of 200 mL of either convalescent plasma or 0.9% saline solution. The primary outcome measure was hospital discharge and/or improvement of ≥ 2 points on the World Health Organisation Blueprint Ordinal Scale for Clinical Improvement by day 28 of enrolment. The trial was stopped early for futility by the Data and Safety Monitoring Board. 103 participants, including 21 HIV positive individuals, were randomized at the time of premature trial termination: 52 in the convalescent plasma and 51 in the placebo group. The primary outcome occurred in 31 participants in the convalescent plasma group and and 32 participants in the placebo group (relative risk 1.03 (95% CI 0.77 to 1.38). Two grade 1 transfusion-related adverse events occurred. Participants who improved clinically received convalescent plasma with a higher median anti-SARS-CoV-2 neutralizing antibody titre compared with those who did not (298 versus 205 AU/mL).

Our study contributes additional evidence for recommendations against the use of convalescent plasma for COVID-19 pneumonia. Safety and feasibility in this population supports future investigation for other indications."

Pre-Existing Conditions and Comorbidities

Journal Articles

Clin Infect Dis: Delayed mortality among solid organ transplant recipients hospitalized for COVID-19 (25 February 2022)

> "Introduction: Most studies of solid organ transplant (SOT) recipients with COVID-19 focus on outcomes within one month of illness onset. Delayed mortality in SOT recipients hospitalized for COVID-19 has not been fully examined.
>
> Methods: We used data from a multicenter registry to calculate mortality by 90 days following initial SARS-CoV-2 detection in SOT recipients hospitalized for COVID-19 and developed multivariable Cox proportional-hazards models to compare risk factors for death by days 28 and 90.
>
> Results: Vital status at day 90 was available for 936 of 1117 (84%) SOT recipients hospitalized for COVID-19: 190 of 936 (20%) died by 28 days and an additional 56 of 246 deaths (23%) occurred between days 29 and 90. Factors associated with mortality by day 90 included: age > 65 years [aHR 1.8 (1.3-2.4), p =<0.001], lung transplant (vs. non-lung transplant) [aHR 1.5 (1.0-2.3), p=0.05], heart failure [aHR 1.9 (1.2-2.9), p=0.006], chronic lung disease [aHR 2.3 (1.5-3.6), p<0.001] and body mass index ≥ 30 kg/m 2 [aHR 1.5 (1.1-2.0), p=0.02]. These associations were similar for mortality by day 28. Compared to diagnosis during early 2020 (March 1-June 19, 2020), diagnosis during late 2020 (June 20-December 31, 2020) was associated with lower mortality by day 28 [aHR 0.7 (0.5-1.0, p=0.04] but not by day 90 [aHR 0.9 (0.7-1.3), p=0.61].
>
> Conclusions: In SOT recipients hospitalized for COVID-19, >20% of deaths occurred between 28 and 90 days following SARS-CoV-2 diagnosis. Future investigations should consider extending follow-up duration to 90 days for more complete mortality assessment."

Clin Infect Dis: Prospective evaluation of COVID-19 vaccine responses across a broad spectrum of immunocompromising conditions: the COVICS study (18 February 2022)

> "Background: We studied humoral responses after COVID-19 vaccination across varying causes of immunodeficiency.
>
> Methods: Prospective study of fully-vaccinated immunocompromised adults (solid organ transplant (SOT), hematologic malignancy, solid cancers, autoimmune conditions, HIV infection) versus non-immunocompromised healthcare-workers (HCW). The primary outcome was the proportion with a reactive test (seropositive) for IgG to SARS-CoV-2 receptor-binding domain. Secondary outcomes were comparisons of antibody levels and their correlation with pseudovirus neutralization titers. Stepwise logistic regression was used to identify factors associated with seropositivity.

Results: 1271 participants enrolled: 1,099 immunocompromised and 172 HCW. Compared to HCW (92.4% seropositive), seropositivity was lower among participants with SOT (30.7%), hematological malignancies (50.0%), autoimmune conditions (79.1%), solid tumors (78.7%), and HIV (79.8%) ($p<0.01$). Factors associated with poor seropositivity included age, greater immunosuppression, time since vaccination, anti-CD20 monoclonal antibodies, and vaccination with BNT162b2 (Pfizer) or adenovirus vector vaccines versus mRNA-1273 (Moderna). mRNA-1273 was associated with higher antibody levels than BNT162b2 or adenovirus vector vaccines, after adjusting for time since vaccination, age, and underlying condition. Antibody levels were strongly correlated with pseudovirus neutralization titers (Spearman $r=0.89$, $p<0.0001$), but in seropositive participants with intermediate antibody levels, neutralization titers were significantly lower in immunocompromised individuals versus HCW.

Conclusion: Antibody responses to COVID-19 vaccines were lowest among SOT and anti-CD20 monoclonal recipients, and recipients of vaccines other than mRNA-1273. Among those with intermediate antibody levels, pseudovirus neutralization titers were lower in immunocompromised patients than HCW. Additional SARS-CoV-2 preventive approaches are needed for immunocompromised persons, which may need to be tailored to the cause of immunodeficiency."

Long COVID and Other Complications

News in Brief

"Five months post-covid, Nicole Murphy's heart rate is still doing strange things — The prevalence of such symptoms has experts projecting a 'tidal wave' of cardiovascular cases related directly and indirectly to the coronavirus" (WP).

"What is long covid? Current understanding about risks, symptoms and recovery" (WP).

"Kaine introduces bill to research and combat long covid, after suffering it himself" (WP).

Long Reads

"They got 'long Covid.' It cost them dearly. Large numbers of Americans are trying — and failing — to get financial assistance as they battle lingering Covid symptoms, an NBC News investigation found" (NBC).

Journal Articles

Eur J Neurol: Neurological outcomes one year after COVID-19 diagnosis: a prospective longitudinal cohort study (03 March 2022)

> "Introduction: Neurological sequelae from COVID-19 may persist after recovery from acute infection. Here, we aimed to describe the natural history of neurological manifestations over one year after COVID-19.
>
> Methods: We performed a prospective, multicentre, longitudinal cohort study in COVID-19 survivors. At 3-month and 1-year follow-up, patients were assessed for neurological impairments by a neurological examination and a standardized test battery including the assessment of hyposmia (16-item Sniffin-Sticks-test, SS-16), cognitive deficits (Montreal Cognitive Assessment<26), and mental health (Hospital Anxiety and Depression Scale, and Post-traumatic Stress Disorder Checklist-5).
>
> Results: Eighty-one patients were evaluated one year after COVID-19, out of which 76/81 (94%) patients completed 3-month and 1-year follow-up. Patients were 54 (47-64) years old and 59% were male. New and persistent neurological disorders were found in 15% (3-months) and 12% (10/81; 1-year). Symptoms at 1-year follow-up were reported by 48/81 (59%) patients, including fatigue (38%), concentration difficulties (25%), forgetfulness (25%), sleep disturbances (22%), myalgia (17%), limb weakness (17%), headache (16%), impaired sensation (16%), and hyposmia (15%). Neurological examination revealed findings in 52/81 (64%) patients without improvement over time (3-months: 61%, p=0.230) including hyposmia (SS-16<13; 51%). Cognitive deficits were apparent in 18%, whereas depression, anxiety, and post-traumatic stress disorders were diagnosed in 6%, 29%, and 10% one year after infection, respectively. These mental and cognitive disorders did not improve since 3-month follow-up (all p>0.05).
>
> Conclusion: Our data indicate that a significant patient number still suffer from neurological sequelae including neuropsychiatric symptoms one year after COVID-19 calling for interdisciplinary management of these patients."

Neurol Neuroimmunol Neuroinflamm: Peripheral Neuropathy Evaluations of Patients With Prolonged Long COVID (01 March 2022)

> "Background and objectives: Recovery from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection appears exponential, leaving a tail of patients reporting various long COVID symptoms including unexplained fatigue/exertional intolerance and dysautonomic and sensory concerns. Indirect evidence links long COVID to incident polyneuropathy affecting the small-fiber (sensory/autonomic) axons.
>
> Methods: We analyzed cross-sectional and longitudinal data from patients with World Health Organization (WHO)-defined long COVID without prior neuropathy history or risks

who were referred for peripheral neuropathy evaluations. We captured standardized symptoms, examinations, objective neurodiagnostic test results, and outcomes, tracking participants for 1.4 years on average.

Results: Among 17 patients (mean age 43.3 years, 69% female, 94% Caucasian, and 19% Latino), 59% had ≥1 test interpretation confirming neuropathy. These included 63% (10/16) of skin biopsies, 17% (2/12) of electrodiagnostic tests and 50% (4/8) of autonomic function tests. One patient was diagnosed with critical illness axonal neuropathy and another with multifocal demyelinating neuropathy 3 weeks after mild COVID, and ≥10 received small-fiber neuropathy diagnoses. Longitudinal improvement averaged 52%, although none reported complete resolution. For treatment, 65% (11/17) received immunotherapies (corticosteroids and/or IV immunoglobulins).

Discussion: Among evaluated patients with long COVID, prolonged, often disabling, small-fiber neuropathy after mild SARS-CoV-2 was most common, beginning within 1 month of COVID-19 onset. Various evidence suggested infection-triggered immune dysregulation as a common mechanism."

Rheumatol Adv Pract: Persistent post-discharge symptoms after COVID-19 in rheumatic and musculoskeletal diseases (17 February 2022)

"Objectives: We aimed to describe persistent symptoms and sequelae in patients with rheumatic and musculoskeletal diseases (RMD) after admission owing to coronavirus disease 2019 (COVID-19), assessing the role of autoimmune rheumatic diseases (ARDs) compared with non-autoimmune rheumatic and musculoskeletal diseases (NARDs) on persistent symptoms and sequelae.

Methods: We performed an observational study including RMD patients who attended a rheumatology clinic in Madrid and required admission owing to COVID-19 (between March and May 2020) and survived. The study began at discharge and ran until October 2020. Main outcomes were persistence of symptoms and sequelae related to COVID-19. The independent variable was the RMD group (ARD and NARD). Covariates included sociodemographics, clinical and treatment data. We ran a multivariate logistic regression model to assess the risk of the main outcomes by RMD group.

Results: We included 105 patients, of whom 51.5% had ARD and 68.57% reported at least one persistent symptom. The most frequent symptoms were dyspnoea, fatigue and chest pain. Sequelae were recorded in 31 patients. These included lung damage in 10.4% of patients, lymphopenia in 10%, a central retinal vein occlusion and an optic neuritis. Two patients died. Eleven patients required re-admission owing to COVID-19 problems (16.7% ARD vs 3.9% NARD; P = 0.053). No statistically significant differences were found between RMD groups in the final models.

Conclusion: Many RMD patients have persistent symptoms, as in other populations. Lung damage is the most frequent sequela. Compared with NARD, ARD does not seem to differ in terms of persistent symptoms or consequences, although ARD might have more re-admissions owing to COVID-19."

J Formos Med Assoc: A multi-disciplinary rehabilitation approach for people surviving severe COVID-19-a case series and literature review (14 February 2022)

"Background/purpose: COronaVIrus Disease 2019 (COVID-19) has caused tremendous casualties and morbidities worldwide. Multisystem manifestations, including muscle weakness, dyspnea, cognitive decline, dysphagia, and dysarthria are frequently reported among critically ill patients. The resultant activity limitations and participation restrictions call for an organized and multidisciplinary approach to rehabilitation. Taiwan had a rapid surge in community infection cases from May to July 2021, and our team established a team-based approach in response to the rehabilitation needs for the in-patients, especially the critically-ill group.

Methods: We built a core treatment team and established a referral pathway for critically ill patients with COVID-19 based on a multidisciplinary approach. The care process and outcomes of a case series of patients who received in-patient rehabilitation after medical stabilization were presented.

Results: Our clinical care module was established according to interim World Health Organization guidance and current research and demonstrated a high degree of feasibility. Five patients with multiple impairments received in-patient rehabilitation and experienced significant functional improvement. We documented improvements in motor function, swallowing function, and activities of daily living after the rehabilitation.

Conclusion: Our clinical experience suggests considerable benefits can be obtained from a well-organized and multidisciplinary rehabilitation approach for severe COVID-19 patients."

J Clin Med: Patterns of Long COVID Symptoms: A Multi-Center Cross Sectional Study (09 February 2022)

"Background: Long COVID has become a burden on healthcare systems worldwide. Research into the etiology and risk factors has been impeded by observing all diverse manifestations as part of a single entity. We aimed to determine patterns of symptoms in convalescing COVID-19 patients.

Methods: Symptomatic patients were recruited from four countries. Data were collected regarding demographics, comorbidities, acute disease and persistent symptoms. Factor analysis was performed to elucidate symptom patterns. Associations of the patterns with patients' characteristics, features of acute disease and effect on daily life were sought.

Results: We included 1027 symptomatic post-COVID individuals in the analysis. The majority of participants were graded as having a non-severe acute COVID-19 (N = 763, 74.3%). We identified six patterns of symptoms: cognitive, pain-syndrome, pulmonary, cardiac, anosmia-dysgeusia and headache. The cognitive pattern was the major symptoms pattern, explaining 26.2% of the variance; the other patterns each explained 6.5-9.5% of the variance. The cognitive pattern was higher in patients who were outpatients during the acute disease. The pain-syndrome pattern was associated with acute disease severity, higher in women and increased with age. The pulmonary pattern was associated with prior lung disease and severe acute disease. Only two of the patterns (cognitive and cardiac) were associated with failure to return to pre-COVID occupational and physical activity status.

Conclusion: Long COVID diverse symptoms can be grouped into six unique patterns. Using these patterns in future research may improve our understanding of pathophysiology and risk factors of persistent COVID, provide homogenous terminology for clinical research, and direct therapeutic interventions."

Pregnancy and Postpartum Period

News in Brief

"Why pregnant people were left behind while vaccines moved at 'warp speed' to help the masses" (KHN).

"Pregnancy-related deaths were already rising in the US. Then COVID arrived and made things worse" (Boston Globe).

Journal Articles

Acta Obstet Gynecol Scand: Management and implications of severe COVID-19 in pregnancy in the UK: data from the UK Obstetric Surveillance System national cohort (25 February 2022)

"Introduction: There is a lack of population level data on risk factors and impact of severe COVID-19 in pregnancy. The aims of this study were to determine the characteristics, and maternal and perinatal outcomes associated with severe COVID-19 in pregnancy compared with those with mild and moderate COVID-19 and to explore the impact of timing of birth.

Material and methods: This was a secondary analysis of a national, prospective cohort study. All pregnant women admitted to hospital in the UK with symptomatic SARS-CoV-2 from March 1, 2020 to October 31, 2021 were included. The severity of maternal infection

(need for high flow or invasive ventilation, intensive care admission or died), pregnancy and perinatal outcomes, and the impact of timing of birth were analyzed using multivariable logistic regression.

Results: Of 4436 pregnant women, 13.9% (n = 616) had severe infection. Women with severe infection were more likely to be aged ≥30 years (adjusted odds ratio [aOR] aged 30-39 1.48, 95% confidence interval [CI] 1.20-1.83), be overweight or obese (aOR 1.73, 95% CI 1.34-2.25 and aOR 2.52 95% CI 1.97-3.23, respectively), be of mixed ethnicity (aOR 1.93, 95% CI 1.17-3.21) or have gestational diabetes (aOR 1.43, 95% CI 1.09-1.87) compared with those with mild or moderate infection. Women with severe infection were more likely to have a pre-labor cesarean birth (aOR 8.84, 95% CI 6.61-11.83), a very or extreme preterm birth (28-31+ weeks' gestation, aOR 18.97, 95% CI 7.78-14.85; <28 weeks' gestation, aOR 12.35, 95% CI 6.34-24.05) and their babies were more likely to be stillborn (aOR 2.51, 95% CI 1.35-4.66) or admitted to a neonatal unit (aOR 11.61, 95% CI 9.28-14.52). Of 112 women with severe infection who were discharged and gave birth at a later admission, the majority gave birth ≥36 weeks (85.7%), noting that three women in this group (2.7%) had a stillbirth.

Conclusions: Severe COVID-19 in pregnancy increases the risk of adverse outcomes. Information to promote uptake of vaccination should specifically target those at greatest risk of severe outcomes. Decisions about timing of birth should be informed by multidisciplinary team discussion; however, our data suggest that women with severe infection who do not require early delivery have mostly good outcomes but that those with severe infection at term may warrant rapid delivery."

Sci Rep: Investigating the association between severity of COVID-19 infection during pregnancy and neonatal outcomes (22 February 2022)

"Pregnant women with COVID-19 require special attention and care, since the infection does not only affect the mother, but also her neonate and adversely affects pregnancy outcomes. The main goal of this retrospective cohort study is to investigate association between the maternal COVID-19 severity and risk of developing adverse neonatal outcomes. Patients were stratified into asymptomatic/mild and moderate to severe COVID-19. The following neonatal outcomes were assessed: gestational age at the time of delivery, birth weight, neonatal infection, neonatal intensive care unit (NICU) admission. The average age of patients was 28.5 ± 1.4 years old and majority were multigravida (74.0%, n = 148). Of total 200 pregnant women with COVID-19, 26.5% (n = 53) had moderate/severe disease and presented with higher incidence of preterm delivery and low birth weight (88.7%, n = 47; p < 0.001). In addition, more than half of the newborns delivered by mothers with severe disease were infected by SARS-COV-2 (58.5%, n = 31) and majority were admitted to the NICU (95.0%, n = 52). Based on the multivariate logistic regression analysis, pregnant women with moderate to severe COVID-19 were at much higher risk of preterm delivery, lower birth weight, neonatal infection, as well as neonatal ICU admission (p < 0.001). In

addition, multigravida women were at higher risk for preterm delivery and lower birth weight (p = 0.017 and p = 0.02; respectively). Appropriate protective measures and early detection of suspected COVID-19 should be addressed for more favorable obstetric outcomes."

Emerg Infect Dis: Increased COVID-19 severity among pregnant patients infected with SARS-CoV-2 Delta variant, France (18 February 2022)

"We conducted a retrospective study of pregnant persons hospitalized for severe acute respiratory syndrome coronavirus 2 infection in France. Delta variant infection had a relative risk of 14.33 for intensive care unit admission and 9.56 for high supplemental oxygen support. The Delta variant might cause more severe illness during pregnancy"

Emerg Infect Dis: Detection of SARS-CoV-2 in Neonatal Autopsy Tissues and Placenta (09 February 2022)

"Severe coronavirus disease in neonates is rare. We analyzed clinical, laboratory, and autopsy findings from a neonate in the United States who was delivered at 25 weeks of gestation and died 4 days after birth; the mother had asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and preeclampsia. We observed severe diffuse alveolar damage and localized SARS-CoV-2 by immunohistochemistry, in situ hybridization, and electron microscopy of the lungs of the neonate. We localized SARS-CoV-2 RNA in neonatal heart and liver vascular endothelium by using in situ hybridization and detected SARS-CoV-2 RNA in neonatal and placental tissues by using reverse transcription PCR. Subgenomic reverse transcription PCR suggested viral replication in lung/airway, heart, and liver. These findings indicate that in utero SARS-CoV-2 transmission contributed to this neonatal death."

Pediatric Population

News in Brief

"Children's mental health takes toll on parents' work performance, new survey shows" (CBS).

The NIH's COVID-19 treatment guidelines now include recommendations for using immunomodulators and antithrombotics for multisystem inflammatory syndrome (MIS-C) in children with (NIH).

Journal Articles

Vaccines

MMWR: Effectiveness of COVID-19 Pfizer-BioNTech BNT162b2 mRNA Vaccination in Preventing COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Nonimmunocompromised Children and Adolescents Aged 5–17 Years — VISION Network, 10 States, April 2021–January 2022 (04 March 2022)

> "What is already known about this topic? Two doses of Pfizer-BioNTech vaccine provided protection against COVID-19 in persons aged 12–17 years during Delta predominance, but data during Omicron predominance and among children aged 5–11 years are lacking.
>
> What is added by this report? Two doses protect against COVID-19–associated emergency department and urgent care encounters among children and adolescents. However, vaccine effectiveness (VE) was lower during Omicron predominance and decreased with time since vaccination; a booster dose restored VE to 81% among adolescents aged 16–17 years. Overall, 2-dose VE against COVID-19–associated hospitalization was 73%–94%.
>
> What are the implications for public health practice? All eligible children and adolescents should remain up to date with recommended COVID-19 vaccinations, including a booster dose for those aged 12–17 years."

MMWR: Safety Monitoring of COVID-19 Vaccine Booster Doses Among Persons Aged 12–17 Years — United States, December 9, 2021–February 20, 2022 (04 March 2022)

> "What is already known about this topic? Adults aged ≥18 years reported adverse reactions less frequently after receipt of a homologous Pfizer-BioNTech COVID-19 booster dose than after the second primary dose.
>
> What is added by this report? Among persons aged 12–17 years, reactions after Pfizer-BioNTech booster vaccination were generally mild to moderate and transient; the frequency of local and systemic reactions reported to v-safe after a booster dose were equal to or slightly higher than after the second primary dose. Myocarditis was less frequently reported after a booster dose than a second primary dose.
>
> What are the implications for public health practice? Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after a homologous Pfizer-BioNTech booster vaccination and that serious adverse events are rare."

JAMA Netw Open: Assessment of Clinical Effectiveness of BNT162b2 COVID-19 Vaccine in US Adolescents (03 March 2022)

> "Question: What is the association between the BNT162b2 COVID-19 vaccine and SARS-CoV-2 positivity among adolescents?
>
> Findings: This case-control study of 542 adolescents was conducted when the Delta variant of SARS-CoV-2 was predominant and within 4 months of the vaccine rollout for adolescents. Overall, the estimated effectiveness of the BNT162b2 vaccine was 91%, with 93% protection against symptomatic infections and 85% effectiveness against asymptomatic infection.
>
> Meaning: These findings suggest that the BNT162b2 vaccine was effective in adolescents within 4 months of immunization, including against infections caused by the Delta variant."

Emerg Infect Dis: Disparities in First Dose COVID-19 Vaccination Coverage among Children 5–11 Years of Age, United States (28 February 2022)

> "We analyzed first-dose coronavirus disease vaccination coverage among US children 5–11 years of age during November–December 2021. Pediatric vaccination coverage varied widely by jurisdiction, age group, and race/ethnicity, and lagged behind vaccination coverage for adolescents aged 12–15 years during the first 2 months of vaccine rollout."

NEJM: Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents (24 February 2022)

> "Background: The increasing incidence of pediatric hospitalizations associated with coronavirus disease 2019 (Covid-19) caused by the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the United States has offered an opportunity to assess the real-world effectiveness of the BNT162b2 messenger RNA vaccine in adolescents between 12 and 18 years of age.
>
> Methods: We used a case-control, test-negative design to assess vaccine effectiveness against Covid-19 resulting in hospitalization, admission to an intensive care unit (ICU), the use of life-supporting interventions (mechanical ventilation, vasopressors, and extracorporeal membrane oxygenation), or death. Between July 1 and October 25, 2021, we screened admission logs for eligible case patients with laboratory-confirmed Covid-19 at 31 hospitals in 23 states. We estimated vaccine effectiveness by comparing the odds of antecedent full vaccination (two doses of BNT162b2) in case patients as compared with two hospital-based control groups: patients who had Covid-19-like symptoms but negative results on testing for SARS-CoV-2 (test-negative) and patients who did not have Covid-19-like symptoms (syndrome-negative).
>
> Results: A total of 445 case patients and 777 controls were enrolled. Overall, 17 case patients (4%) and 282 controls (36%) had been fully vaccinated. Of the case patients, 180

(40%) were admitted to the ICU, and 127 (29%) required life support; only 2 patients in the ICU had been fully vaccinated. The overall effectiveness of the BNT162b2 vaccine against hospitalization for Covid-19 was 94% (95% confidence interval [CI], 90 to 96); the effectiveness was 95% (95% CI, 91 to 97) among test-negative controls and 94% (95% CI, 89 to 96) among syndrome-negative controls. The effectiveness was 98% against ICU admission and 98% against Covid-19 resulting in the receipt of life support. All 7 deaths occurred in patients who were unvaccinated.

Conclusions: Among hospitalized adolescent patients, two doses of the BNT162b2 vaccine were highly effective against Covid-19-related hospitalization and ICU admission or the receipt of life support."

Other Literature

Nutr Clin Pract: Increased nutrition risk at admission is associated with longer hospitalization in children and adolescents with COVID-19 (28 February 2022)

"Background: We investigated the association of nutritional risk and inflammatory marker level with length of stay (LOS) in children and adolescents hospitalized for COVID-19 infection in two pediatric teaching hospitals in a developing country.

Methods: This was a cross-sectional analytical retrospective study performed in two pediatric hospitals. We included the data from all children and adolescents who were hospitalized with a SARS-CoV-2 infection between March and December 2020. Demographic, anthropometric, clinical, and laboratory data were extracted from electronic medical records. Nutritional risk was assessed according to the STRONGkids tool within 24 hours of admission and was categorized into two levels: ≥4 (high risk) and <4 (moderate or low risk). Means or medians were compared between nutritional risk groups using the t test and Mann-Whitney U test, respectively. The association of nutritional risk and inflammatory markers with LOS was estimated using the Kaplan-Meier method and log-rank test. Cox proportional-hazard and linear regression models were performed, and adjusted for sex, age, and respiratory symptoms.

Results: From a total of 73 patients, 20 (27.4%) had a STRONGkids score ≥4 at admission, which was associated with a longer LOS even after adjusting (β = 12.30; 1.74-22.9 95% CI; P = 0.023). The same association was observed between LOS and all laboratory markers except for D-dimer.

Conclusion: Among children and adolescents with COVID-19, a STRONGkids score ≥4 at admission, lower values of albumin, lymphocytes, and hemoglobin, and higher CRP values were associated with longer LOS."

Clin Infect Dis: Overcoming COVID-19 Investigators. Measurement of SARS-CoV-2 antigens in plasma of pediatric patients with acute COVID-19 or MIS-C using an ultrasensitive and quantitative immunoassay (25 February 2022)

> "Background: Detection of SARS-CoV-2 antigens in blood has high sensitivity in adults with acute COVID-19, but sensitivity in pediatric patients is unclear. Recent data suggest that persistent SARS-CoV-2 spike antigenemia may contribute to multisystem inflammatory syndrome in children (MIS-C). We quantified SARS-CoV-2 nucleocapsid (N) and spike (S) antigens in blood of pediatric patients with either acute COVID-19 or MIS-C using ultrasensitive immunoassays (Meso Scale Discovery).
>
> Methods: Plasma was collected from inpatients (<21 years) enrolled across 15 hospitals in 15 US states. Acute COVID-19 patients (n=36) had a range of disease severity and positive nasopharyngeal SARS-CoV-2 RT-PCR within 24 hours of blood collection. Patients with MIS-C (n=53) met CDC criteria and tested positive for SARS-CoV-2 (RT-PCR or serology). Controls were patients pre-COVID-19 (n=67) or within 24h of negative RT-PCR (n=43).
>
> Results: Specificities of N and S assays were 95-97% and 100%, respectively. In acute COVID-19 patients, N/S plasma assays had 89%/64% sensitivity, respectively; sensitivity in patients with concurrent nasopharyngeal swab cycle threshold (Ct) < 35 were 93%/63%. Antigen concentrations ranged from 1.28-3,844 pg/mL (N) and 1.65-1,071 pg/mL (S) and correlated with disease severity. In MIS-C, antigens were detected in 3/53 (5.7%) samples (3 N-positive: 1.7, 1.9, 121.1 pg/mL; 1 S-positive: 2.3 pg/mL); the patient with highest N had positive nasopharyngeal RT-PCR (Ct 22.3) concurrent with blood draw.
>
> Conclusions: Ultrasensitive blood SARS-CoV-2 antigen measurement has high diagnostic yield in children with acute COVID-19. Antigens were undetectable in most MIS-C patients, suggesting that persistent antigenemia is not a common contributor to MIS-C pathogenesis."

MMWR: Pediatric Emergency Department Visits Before and During the COVID-19 Pandemic — United States, January 2019–January 2022 (25 February 2022)

> "What is already known about this topic? Health seeking behavior has changed during the COVID-19 pandemic.
>
> What is added by this report? Compared with 2019, overall pediatric emergency department visits decreased by 51%, 22%, and 23% during 2020, 2021, and January 2022, respectively. COVID-19 visits predominated across all pediatric ages; visits for other respiratory illnesses mostly declined. Number and proportion of visits increased for certain injuries (e.g., firearm injuries, self-harm, and drug poisonings), some chronic diseases, and behavioral health concerns, with variations by age group.

What are the implications for public health practice? Health care providers and families should remain vigilant for potential indirect impacts of the COVID-19 pandemic, including health conditions resulting from delayed care, and increasing emotional distress and behavioral health concerns among children and adolescents."

See also: Mental Health Surveillance Among Children — United States, 2013–2019

MMWR: Pediatric Emergency Department Visits Associated with Mental Health Conditions Before and During the COVID-19 Pandemic — United States, January 2019–January 2022 (25 February 2022)

"What is already known about this topic? The proportion of pediatric emergency department (ED) visits for mental health conditions (MHCs) increased during 2020.

What is added by this report? Weekly ED visits among adolescent females (aged 12–17 years) increased for two MHCs (eating and tic disorders) during 2020, four (depression, eating, tic, and obsessive-compulsive disorders) during 2021, and five (anxiety; trauma and stressor-related; eating; tic; and obsessive-compulsive disorders) and overall MHC visits during January 2022, compared with 2019. The proportion of ED visits with eating disorders doubled among adolescent females; those for tic disorders approximately tripled during the pandemic.

What are the implications for public health practice? Early identification and expanded evidence-based prevention and intervention strategies are critical to improving pediatric mental health, especially among adolescent females, who might have increased need."

See also: Mental Health Surveillance Among Children — United States, 2013–2019

Lancet Child Adolesc Health: Global, regional, and national minimum estimates of children affected by COVID-19-associated orphanhood and caregiver death, by age and family circumstance up to Oct 31, 2021: an updated modelling study (24 February 2022)

"Background: In the 6 months following our estimates from March 1, 2020, to April 30, 2021, the proliferation of new coronavirus variants, updated mortality data, and disparities in vaccine access increased the amount of children experiencing COVID-19-associated orphanhood. To inform responses, we aimed to model the increases in numbers of children affected by COVID-19-associated orphanhood and caregiver death, as well as the cumulative orphanhood age-group distribution and circumstance (maternal or paternal orphanhood).

Methods: We used updated excess mortality and fertility data to model increases in minimum estimates of COVID-19-associated orphanhood and caregiver deaths from our original study period of March 1, 2020-April 30, 2021, to include the new period of May 1-Oct 31, 2021, for 21 countries. Orphanhood was defined as the death of one or both

parents; primary caregiver loss included parental death or the death of one or both custodial grandparents; and secondary caregiver loss included co-residing grandparents or kin. We used logistic regression and further incorporated a fixed effect for western European countries into our previous model to avoid over-predicting caregiver loss in that region. For the entire 20-month period, we grouped children by age (0-4 years, 5-9 years, and 10-17 years) and maternal or paternal orphanhood, using fertility contributions, and we modelled global and regional extrapolations of numbers of orphans. 95% credible intervals (CrIs) are given for all estimates.

Findings: The number of children affected by COVID-19-associated orphanhood and caregiver death is estimated to have increased by 90·0% (95% CrI 89·7-90·4) from April 30 to Oct 31, 2021, from 2 737 300 (95% CrI 1 976 100-2 987 000) to 5 200 300 (3 619 400-5 731 400). Between March 1, 2020, and Oct 31, 2021, 491 300 (95% CrI 485 100-497 900) children aged 0-4 years, 736 800 (726 900-746 500) children aged 5-9 years, and 2 146 700 (2 120 900-2 174 200) children aged 10-17 years are estimated to have experienced COVID-19-associated orphanhood. Globally, 76·5% (95% CrI 76·3-76·7) of children were paternal orphans, whereas 23·5% (23·3-23·7) were maternal orphans. In each age group and region, the prevalence of paternal orphanhood exceeded that of maternal orphanhood.

Interpretation: Our findings show that numbers of children affected by COVID-19-associated orphanhood and caregiver death almost doubled in 6 months compared with the amount after the first 14 months of the pandemic. Over the entire 20-month period, 5·0 million COVID-19 deaths meant that 5·2 million children lost a parent or caregiver. Our data on children's ages and circumstances should support pandemic response planning for children globally."

Lancet Child Adolesc Health: Reported cases of multisystem inflammatory syndrome in children aged 12–20 years in the USA who received a COVID-19 vaccine, December, 2020, through August, 2021: a surveillance investigation (22 February 2022)

"Background: Multisystem inflammatory syndrome in children (MIS-C) is a hyperinflammatory condition associated with antecedent SARS-CoV-2 infection. In the USA, reporting of MIS-C after vaccination is required under COVID-19 vaccine emergency use authorisations. We aimed to investigate reports of individuals aged 12–20 years with MIS-C after COVID-19 vaccination reported to passive surveillance systems or through clinician outreach to the US Centers for Disease Control and Prevention (CDC).

Methods: In this surveillance activity, we investigated potential cases of MIS-C after COVID-19 vaccination reported to CDC's MIS-C national surveillance system, the Vaccine Adverse Event Reporting System (co-administered by CDC and the US Food and Drug Administration), and CDC's Clinical Immunization Safety Assessment Project. A multidisciplinary team adjudicated cases by use of the CDC MIS-C definition. Any positive

SARS-CoV-2 serology test satisfied case criteria; although anti-nucleocapsid antibodies indicate previous SARS-CoV-2 infection, anti-spike protein antibodies indicate either past or recent infection or COVID-19 vaccination. We describe the demographic and clinical features of cases, stratified by laboratory evidence of SARS-CoV-2 infection. To calculate the reporting rate of MIS-C, we divided the count of all individuals meeting the MIS-C case definition, and of those without evidence of SARS-CoV-2 infection, by the number of individuals aged 12–20 years in the USA who received one or more COVID-19 vaccine doses up to Aug 31, 2021, obtained from CDC national vaccine surveillance data.

Findings: Using surveillance results from Dec 14, 2020, to Aug 31, 2021, we identified 21 individuals with MIS-C after COVID-19 vaccination. Of these 21 individuals, median age was 16 years (range 12–20); 13 (62%) were male and eight (38%) were female. All 21 were hospitalised: 12 (57%) were admitted to an intensive care unit and all were discharged home. 15 (71%) of 21 individuals had laboratory evidence of past or recent SARS-CoV-2 infection, and six (29%) did not. As of Aug 31, 2021, 21 335 331 individuals aged 12–20 years had received one or more doses of a COVID-19 vaccine, making the overall reporting rate for MIS-C after vaccination 1·0 case per million individuals receiving one or more doses in this age group. The reporting rate in only those without evidence of SARS-CoV-2 infection was 0·3 cases per million vaccinated individuals.

Interpretation: Here, we describe a small number of individuals with MIS-C who had received one or more doses of a COVID-19 vaccine before illness onset; the contribution of vaccination to these illnesses is unknown. Our findings suggest that MIS-C after COVID-19 vaccination is rare. Continued reporting of potential cases and surveillance for MIS-C illnesses after COVID-19 vaccination is warranted."

JAMA Pediatr: Severity of Hospitalizations from SARS-CoV-2 vs Influenza and Respiratory Syncytial Virus Infection in Children Aged 5 to 11 Years in 11 US States (21 February 2022)

"This cross-sectional study investigates the severity of hospitalizations from SARS-CoV-2 infection compared with that of influenza and respiratory syncytial virus in children aged 5 to 11 years in 11 US states….

This cross-sectional study revealed that during the winter of 2020-2021, for children aged 5 to 11 years, there was 1 MIS-C hospitalization for every COVID-19 hospitalization. This finding suggests that MIS-C may not be as rare of a COVID-19 sequela as previously thought. Other long-term COVID-19 complications may also be of concern for children aged 5 to 11 years. Although rarer than influenza infection, the extreme severity of MIS-C made the total economic and health burden of COVID-19 infection combined with MIS-C just as high as that of past influenza outbreaks."

Healthcare Workers

News in Brief

"This hospital tried to save a man with covid. Then the threats started" (WP).

Journal Articles

Int J Environ Res Public Health: "Well, I Signed Up to Be a Soldier; I Have Been Trained and Equipped Well": Exploring Healthcare Workers' Experiences during COVID-19 Organizational Changes in Singapore, from the First Wave to the Path towards Endemicity (21 February 2022)

> "Background: As COVID-19 transmission continues despite vaccination programs, healthcare workers (HCWs) face an ongoing pandemic response. We explore the effects of this on (1) Heartware, by which we refer to morale and commitment of HCWs; and identify how to improve (2) Hardware, or ways of enabling operational safety and functioning.
>
> Methods: Qualitative e-diary entries were shared by HCWs during the early phases of the outbreak in Singapore from June to August 2020. Data were collected via an online survey of n = 3616 HCWs of all cadres. Nine institutions-restructured hospitals (n = 5), affiliated primary partners (n = 2) and hospices (n = 2)-participated. Applied thematic analysis was undertaken and organized according to Heartware and Hardware.
>
> Results: n = 663 (18%) HCWs submitted a qualitative entry. Dominant themes undermining (1) Heartware consisted of burnout from being overworked and emotional exhaustion and at times feeling a lack of appreciation or support at work. The most common themes overriding morale breakers were a stoic acceptance to fight, adjust and hold the line, coupled with motivation from engaging leadership and supportive colleagues. The biggest barrier in (2) Hardware analysis related to sub-optimal segregation strategies within wards and designing better protocols for case detection, triage, and admissions criteria. Overall, the most cited enabler was the timely and well-planned provision of Personal Protective Equipment (PPE) for front-liners, though scope for scale-up was called for by those not considered frontline. Analysis maps internal organizational functioning to wider external public and policy-related narratives.
>
> Conclusions: COVID-19 surges are becoming endemic rather than exceptional events. System elasticity needs to build on known pillars coupling improving safety and care delivery with improving HCW morale. Accordingly, a model capturing such facets of Adaptive Pandemic Response derived from our data analyses is described. HCW burnout must be urgently addressed, and health systems moved away from reactive "wartime" response configurations."

Int J Environ Res Public Health: Burnout Syndrome in a Military Tertiary Hospital Staff during the COVID-19 Contingency (16 February 2022)

> "Background: Burnout syndrome (BOS) is defined as a psychological state of physical and mental fatigue associated with work. The COVID-19 pandemic greatly impacted the physical and mental wellbeing of health professionals. The objective of this work was to determine the impact on personnel, monitoring the frequency of BOS throughout the pandemic.
>
> Methods: The Maslach Burnout Inventory (MBI) was self-applied in four periods of the pandemic according to sociodemographic and employment characteristics. In this study, all hospital personnel were included; the association of BOS with sex, age, type of participant (civilian or military), military rank and profession was analyzed.
>
> Results: The frequency of BOS was 2.4% (start of the pandemic), 7.9% (peak of the first wave), 3.7% (end of the first wave) and 3.6% (peak of the third wave). Emotional exhaustion (EE) was the most affected factor, and the groups most affected were men under 30 years of age, civilians, chiefs and doctors, especially undergraduate medical doctors and specialty resident doctors, and nursing personnel were less affected.
>
> Conclusions: The low BOS levels show that the containment measures and military training implemented by the hospital authorities were effective, although the chief personnel were more affected in the first wave. It is probable that this combination allowed the containment of BOS, which was not observed in civilians."

Disaster Med Public Health Prep: The Challenges of Nurse Redeployment and Opportunities for Leadership during COVID-19 Pandemic (14 February 2022)

> "Objective: Literature has previously shown that redeployment has been widely implemented to build capacity, but little focused on nurses. This study aims to manage redeployment more effectively by capturing and scrutinizing nurses' redeployment experiences.
>
> Methods: A cross-sectional short and structured interviews were conducted. Data was analysed using Braun and Clarkes Six Step Thematic Analysis approach.
>
> Results: 55 interviews were conducted, predominantly from women (85%, N=47), over the age of 45 years (45%, N=25) in the role of Specialist Nurse or Staff Nurse (78%, N=43). Five critical themes emerged, willingness to work in redeployed role, poor communication, stress and anxiety, feelings of being unsupported and abandoned, and positive experiences despite challenging circumstances.
>
> Conclusions: Nurses in redeployed roles were susceptible to stress and anxiety and were seeking dedicated leadership as they worked during a pandemic with the additional challenge of unfamiliar workspaces and colleagues. Nurses play a major role in the

> resilience of healthcare service, which cannot be achieved without a comprehensive resilience strategy. Healthcare organisations are required to develop strategies and policies and enforcement measures to ensure that staff are well empowered and protected not just during potential redeployment but also in their daily operations."

Disparities and Health Equity

News in Brief

Long Reads

STATnews has a 2-part special report on systemic racism in medicine: "20 years ago, a landmark report spotlighted systemic racism in medicine. Why has so little changed?" (STAT part 1) and "The nation hasn't made much progress on health equity. These leaders forged ahead anyway" (STAT part 2).

Journal Articles

MMWR: Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022 (04 March 2022)

> "What is already known about this topic? COVID-19 incidence and mortality are higher in rural than in urban communities. Disparities in COVID-19 vaccination coverage between urban and rural communities have been recognized.
>
> What is added by this report? COVID-19 vaccination coverage with the first dose of the primary vaccination series was lower in rural (58.5%) than in urban counties (75.4%); disparities have increased more than twofold since April 2021. Receipt of booster or additional doses was similarly low in both rural and urban counties.
>
> What are the implications for public health practice? Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19–related illness and death in the United States."

Lancet: Quantifying the effects of the COVID-19 pandemic on gender equality on health, social, and economic indicators: a comprehensive review of data from March, 2020, to September, 2021 (02 March 2022)

> "Background: Gender is emerging as a significant factor in the social, economic, and health effects of COVID-19. However, most existing studies have focused on its direct impact on

health. Here, we aimed to explore the indirect effects of COVID-19 on gender disparities globally.

Methods: We reviewed publicly available datasets with information on indicators related to vaccine hesitancy and uptake, health care services, economic and work-related concerns, education, and safety at home and in the community. We used mixed effects regression, Gaussian process regression, and bootstrapping to synthesise all data sources. We accounted for uncertainty in the underlying data and modelling process. We then used mixed effects logistic regression to explore gender gaps globally and by region.

Findings: Between March, 2020, and September, 2021, women were more likely to report employment loss (26·0% [95% uncertainty interval 23·8–28·8, by September, 2021) than men (20·4% [18·2–22·9], by September, 2021), as well as forgoing work to care for others (ratio of women to men: 1·8 by March, 2020, and 2·4 by September, 2021). Women and girls were 1·21 times (1·20–1·21) more likely than men and boys to report dropping out of school for reasons other than school closures. Women were also 1·23 (1·22–1·23) times more likely than men to report that gender-based violence had increased during the pandemic. By September 2021, women and men did not differ significantly in vaccine hesitancy or uptake.

Interpretation: The most significant gender gaps identified in our study show intensified levels of pre-existing widespread inequalities between women and men during the COVID-19 pandemic. Political and social leaders should prioritise policies that enable and encourage women to participate in the labour force and continue their education, thereby equipping and enabling them with greater ability to overcome the barriers they face."

NEJM: Reliever-Triggered Inhaled Glucocorticoid in Black and Latinx Adults with Asthma (26 February 2022)

"Background: Black and Latinx patients bear a disproportionate burden of asthma. Efforts to reduce the disproportionate morbidity have been mostly unsuccessful, and guideline recommendations have not been based on studies in these populations.

Methods: In this pragmatic, open-label trial, we randomly assigned Black and Latinx adults with moderate-to-severe asthma to use a patient-activated, reliever-triggered inhaled glucocorticoid strategy (beclomethasone dipropionate, 80 µg) plus usual care (intervention) or to continue usual care. Participants had one instructional visit followed by 15 monthly questionnaires. The primary end point was the annualized rate of severe asthma exacerbations. Secondary end points included monthly asthma control as measured with the Asthma Control Test (ACT; range, 5 [poor] to 25 [complete control]), quality of life as measured with the Asthma Symptom Utility Index (ASUI; range, 0 to 1, with lower scores indicating greater impairment), and participant-reported missed days of work, school, or usual activities. Safety was also assessed.

Results: Of 1201 adults (603 Black and 598 Latinx), 600 were assigned to the intervention group and 601 to the usual-care group. The annualized rate of severe asthma exacerbations was 0.69 (95% confidence interval [CI], 0.61 to 0.78) in the intervention group and 0.82 (95% CI 0.73 to 0.92) in the usual-care group (hazard ratio, 0.85; 95% CI, 0.72 to 0.999; P = 0.048). ACT scores increased by 3.4 points (95% CI 3.1 to 3.6) in the intervention group and by 2.5 points (95% CI, 2.3 to 2.8) in the usual-care group (difference, 0.9; 95% CI, 0.5 to 1.2); ASUI scores increased by 0.12 points (95% CI, 0.11 to 0.13) and 0.08 points (95% CI, 0.07 to 0.09), respectively (difference, 0.04; 95% CI, 0.02 to 0.05). The annualized rate of missed days was 13.4 in the intervention group and 16.8 in the usual-care group (rate ratio, 0.80; 95% CI, 0.67 to 0.95). Serious adverse events occurred in 12.2% of the participants, with an even distribution between the groups.

Conclusions: Among Black and Latinx adults with moderate-to-severe asthma, provision of an inhaled glucocorticoid and one-time instruction on its use, added to usual care, led to a lower rate of severe asthma exacerbations."

Mental Health and Wellness

Journal Articles

PLoS One: Perceptions of green space usage, abundance, and quality of green space were associated with better mental health during the COVID-19 pandemic among residents of Denver (02 March 2022)

"Background: The COVID-19 pandemic has impacted both physical and mental health. This study aimed to understand whether exposure to green space buffered against stress and distress during the COVID-19 pandemic while taking into account significant stressors of the pandemic.

Methods: We leveraged a cross-sectional survey on green space exposure and mental health among residents of Denver, CO that ran from November 2019 through January 2021. We measured objective green space as the average NDVI (normalized difference vegetation index) from aerial imagery within 300m and 500m of the participant's residence. Perceived green space was measured through Likert scores on five questions about vegetation near the home that captured perceived abundance, visibility, access, usage, and quality of green space. We used generalized linear models to assess the relationship between each green space exposure variable and perceived stress (PSS-4), depression (CES-D-10), or anxiety (MMPI-2) adjusted for sociodemographic and COVID-19 impact variables.

Results: We found significantly higher depression scores for all covid periods compared to the "before covid" period, and significantly higher anxiety scores during the "fall wave" compared to earlier periods. Adjusted for sociodemographic and pandemic stressors, we found that spending a lot of time in green space (usage) was significantly associated with lower anxiety and depression. We also observed significantly lower depression scores associated with NDVI in both buffers (objective abundance) and significantly lower anxiety scores with perceived abundance of green space. There was some evidence of lower anxiety scores for people reporting having high quality green spaces near the home (quality). We did not observe significant associations for any green space metric and perceived stress after adjustment for confounding variables.

Conclusion: Our work provides further evidence of mental health benefits associated with green space exposure during the COVID-19 pandemic even after adjustment for sociodemographic variables and significant pandemic-related stressors."

JAMA: Association of COVID-19 Acute Respiratory Distress Syndrome With Symptoms of Posttraumatic Stress Disorder in Family Members After ICU Discharge (18 February 2022)

"Question: Is the risk of posttraumatic stress disorder (PTSD) symptoms in family members of intensive care unit (ICU) patients with acute respiratory distress syndrome (ARDS) due to COVID-19 different from that of family members of patients with non–COVID-19 ARDS?

Findings: In a prospective cohort study of 517 family members of ICU patients, PTSD-related symptoms at 90 days after ICU discharge were significantly more common in family members of patients with COVID-19 ARDS compared with non–COVID-19 ARDS (35% vs 19%). In a multivariable analysis adjusting for age, sex, and level of social support, COVID-19 ARDS was independently associated with PTSD-related symptoms in family members (odds ratio, 2.05).

Meaning: ARDS due to COVID-19 was associated with a greater risk-adjusted rate of PTSD symptoms among family members compared with ARDS from other causes."

Special Topic: Climate Change and Health

News in Brief

"5 takeaways from the latest United Nations climate change report: Monday's IPCC report is a warning letter to the world. Here's what you need to know from the more than 3,500-page document" (WP; see also full-text IPCC report, noted below).

Interested in literature on how climate change impacts human health? The Climate Change and Human Health Literature Portal from NIH's National Institute of Environmental Health Sciences is an "integrated, curated bibliographic database of global peer-reviewed research and gray literature on the science of climate impacts on human health" (NIEHS).

Special Reports and Other Resources

IPCC: AR6 Climate Change 2022: Impacts, Adaptation and Vulnerability (28 February 2022)

> "The Working Group II contribution to the IPCC Sixth Assessment Report assesses the impacts of climate change, looking at ecosystems, biodiversity, and human communities at global and regional levels. It also reviews vulnerabilities and the capacities and limits of the natural world and human societies to adapt to climate change….
>
> The cumulative scientific evidence is unequivocal: Climate change is a threat to human well-being and planetary health. Any further delay in concerted anticipatory global action on adaptation and mitigation will miss a brief and rapidly closing window of opportunity to secure a liveable and sustainable future for all."

ASPR TRACIE: Climate Change Resilience and Healthcare System Considerations [pdf] (February 2022)

> "Climate change continues to negatively impact national security, environmental stability, and human health conditions. This document provides an overview of climate trends in the U.S., outlining the impacts of climate-related illness and injury on health system operations, care delivery, and patient surge. It touches on the importance of bolstering healthcare infrastructure resilience, facility hardening, and highlights three areas being affected by various elements of climate change."
>
> See also: Topic Collection

Journal Articles

Int J Environ Res Public Health: Identifying Types of Eco-Anxiety, Eco-Guilt, Eco-Grief, and Eco-Coping in a Climate-Sensitive Population: A Qualitative Study (21 February 2022)

> "Background: Climate change is one of the greatest challenges of the 21st century and it can affect mental health either directly through the experience of environmental traumas or indirectly through the experience of emotional distress and anxiety about the future. However, it is not clear what possible subtypes of the emerging "psychoterratic" syndromes such as eco-anxiety, eco-guilt, and eco-grief exist, how much distress they may cause, and to what extent they facilitate ecofriendly behavior.

Methods: We analyzed semi-structured interviews (N = 17) focusing on the thoughts, emotions, and behaviors related to climate change by using a combination of inductive and deductive qualitative methods.

Results and conclusions: The interviews revealed six eco-anxiety components, eight types of eco-guilt, and two types of eco-grief that help to understand the multifactorial nature of these phenomena. The six categories of coping strategies are in line with traditional coping models, and they are linked in various ways to pro-environmental behavior and the management of negative emotions. The results can help practitioners to gain a deeper understanding of emotions related to climate change and how to cope with them, and researchers to develop comprehensive measurement tools to assess these emotions."

Curr Obes Rep: The COVID-19, Obesity, and Food Insecurity Syndemic (09 February 2022)

"Purpose of review: To introduce and provide evidence for the new Syndemic of COVID-19, Obesity, and Food Insecurity and propose strategies for mitigating its impact, particularly among vulnerable populations.

Recent findings: The COVID-19 pandemic has exacerbated obesity, food insecurity, and the existing inequities in the essential workforce. Food insecurity is driven by unsustainable dietary patterns and is associated with higher rates of obesity, which increases the risk of COVID-19 infections, hospitalizations, and deaths. The COVID-19 pandemic has disproportionately impacted the essential food supply chain workforce. Strengthening the social safety net and expanding worker protections will increase food security and secure livelihoods during and beyond the scope of the COVID-19 pandemic. Strengthening local and regional food systems provides a common solution to both the new Syndemic of COVID-19, Obesity, and Food Insecurity and the Global Syndemic of Obesity, Undernutrition, and Climate Change by promoting sustainable food production and consumption, and prioritizing the food supply chain workforce."

See also: How Can We Act to Mitigate the Global Syndemic of Obesity, Undernutrition, and Climate Change?

Int J Environ Res Public Health: Climate Change and Zoonoses: A Review of Concepts, Definitions, and Bibliometrics (14 January 2022)

"Climate change can have a complex impact that also influences human and animal health. For example, climate change alters the conditions for pathogens and vectors of zoonotic diseases. Signs of this are the increasing spread of the West Nile and Usutu viruses and the establishment of new vector species, such as specific mosquito and tick species, in Europe and other parts of the world. With these changes come new challenges for maintaining human and animal health. This paper reports on an analysis of the literature focused on a bibliometric analysis of the Scopus database and VOSviewer software for creating

visualization maps which identifies the zoonotic health risks for humans and animals caused by climate change. The sources retained for the analysis totaled 428 and different thresholds (N) were established for each item varying from N 5 to 10. The main findings are as follows: First, published documents increased in 2009-2015 peaking in 2020. Second, the primary sources have changed since 2018, partly attributable to the increase in human health concerns due to human-to-human transmission. Third, the USA, the UK, Canada, Australia, Italy, and Germany perform most zoonosis research. For instance, sixty documents and only 17 countries analyzed for co-authorship analysis met the threshold led by the USA; the top four author keywords were "climate change", "zoonosis", "epidemiology", and "one health;" the USA, the UK, Germany, and Spain led the link strength (inter-collaboration); the author keywords showed that 37 out of the 1023 keywords met the threshold, and the authors' keyword's largest node of the bibliometric map contains the following: infectious diseases, emerging diseases, disease ecology, one health, surveillance, transmission, and wildlife. Finally, zoonotic diseases, which were documented in the literature in the past, have evolved, especially during the years 2010-2015, as evidenced by the sharp augmentation of publications addressing ad-hoc events and peaking in 2020 with the COVID-19 outbreak."

Other Infectious Diseases and Public Health Threats

News in Brief

"NIH orders sweeping review of potentially risky experiments on viruses and other pathogens" (WP; see also: NIH statement).

"Novel antibiotic shows success in treatment of plague and melioidosis" (GBD).

"Highly contagious bird flu circulating in DC region is not a danger to humans, officials say" (WP).

For the first time since 2009, there are reported cases of Lassa fever in the United Kingdom (WHO).

"In new setback for eradication campaign, poliovirus from Pakistan shows up in Africa" (Science).

"The three largest U.S. drug distributors and drugmaker Johnson & Johnson have agreed to finalize a proposed $26 billion settlement resolving claims by states and local governments that they helped fuel the U.S. opioid epidemic" (Reuters).

Meanwhile… "Sacklers agree to $6 billion Purdue bankruptcy settlement over opioid crisis" (STAT).

Journal Articles

Lancet Infect Dis: Measuring the effects of COVID-19-related disruption on dengue transmission in southeast Asia and Latin America: a statistical modelling study (02 March 2022)

> "Background: The COVID-19 pandemic has resulted in unprecedented disruption to society, which indirectly affects infectious disease dynamics. We aimed to assess the effects of COVID-19-related disruption on dengue, a major expanding acute public health threat, in southeast Asia and Latin America.
>
> Methods: We assembled data on monthly dengue incidence from WHO weekly reports, climatic data from ERA5, and population variables from WorldPop for 23 countries between January, 2014 and December, 2019 and fit a Bayesian regression model to explain and predict seasonal and multi-year dengue cycles. We compared model predictions with reported dengue data January to December, 2020, and assessed if deviations from projected incidence since March, 2020 are associated with specific public health and social measures (from the Oxford Coronavirus Government Response Tracer database) or human movement behaviours (as measured by Google mobility reports).
>
> Findings: We found a consistent, prolonged decline in dengue incidence across many dengue-endemic regions that began in March, 2020 (2·28 million cases in 2020 vs 4·08 million cases in 2019; a 44·1% decrease). We found a strong association between COVID-19-related disruption (as measured independently by public health and social measures and human movement behaviours) and reduced dengue risk, even after taking into account other drivers of dengue cycles including climatic and host immunity (relative risk 0·01–0·17, p<0·01). Measures related to the closure of schools and reduced time spent in non-residential areas had the strongest evidence of association with reduced dengue risk, but high collinearity between covariates made specific attribution challenging. Overall, we estimate that 0·72 million (95% CI 0·12–1·47) fewer dengue cases occurred in 2020 potentially attributable to COVID-19-related disruption.
>
> Interpretation: In most countries, COVID-19-related disruption led to historically low dengue incidence in 2020. Continuous monitoring of dengue incidence as COVID-19-related restrictions are relaxed will be important and could give new insights into transmission processes and intervention options."

NEJM: Mortality from Congenital Zika Syndrome - Nationwide Cohort Study in Brazil (24 February 2022)

> "Background: Prenatal exposure to Zika virus has potential teratogenic effects, with a wide spectrum of clinical presentation referred to as congenital Zika syndrome. Data on survival among children with congenital Zika syndrome are limited.

Methods: In this population-based cohort study, we used linked, routinely collected data in Brazil, from January 2015 through December 2018, to estimate mortality among live-born children with congenital Zika syndrome as compared with those without the syndrome. Kaplan-Meier curves and survival models were assessed with adjustment for confounding and with stratification according to gestational age, birth weight, and status of being small for gestational age.

Results: A total of 11,481,215 live-born children were followed to 36 months of age. The mortality rate was 52.6 deaths (95% confidence interval [CI], 47.6 to 58.0) per 1000 person-years among live-born children with congenital Zika syndrome, as compared with 5.6 deaths (95% CI, 5.6 to 5.7) per 1000 person-years among those without the syndrome. The mortality rate ratio among live-born children with congenital Zika syndrome, as compared with those without the syndrome, was 11.3 (95% CI, 10.2 to 12.4). Among infants born before 32 weeks of gestation or with a birth weight of less than 1500 g, the risks of death were similar regardless of congenital Zika syndrome status. Among infants born at term, those with congenital Zika syndrome were 14.3 times (95% CI, 12.4 to 16.4) as likely to die as those without the syndrome (mortality rate, 38.4 vs. 2.7 deaths per 1000 person-years). Among infants with a birth weight of 2500 g or greater, those with congenital Zika syndrome were 12.9 times (95% CI, 10.9 to 15.3) as likely to die as those without the syndrome (mortality rate, 32.6 vs. 2.5 deaths per 1000 person-years). The burden of congenital anomalies, diseases of the nervous system, and infectious diseases as recorded causes of deaths was higher among live-born children with congenital Zika syndrome than among those without the syndrome.

Conclusions: The risk of death was higher among live-born children with congenital Zika syndrome than among those without the syndrome and persisted throughout the first 3 years of life."

Emerg Infect Dis: Overseas Treatment of Latent Tuberculosis Infection in US–Bound Immigrants (16 February 2022)

"Seventy percent of tuberculosis (TB) cases in the United States occur among non–US-born persons; cases usually result from reactivation of latent TB infection (LTBI) likely acquired before the person's US arrival. We conducted a prospective study among US immigrant visa applicants undergoing the required overseas medical examination in Vietnam. Consenting applicants >15 years of age were offered an interferon-γ release assay (IGRA); those 12–14 years of age received an IGRA as part of the required examination. Eligible participants were offered LTBI treatment with 12 doses of weekly isoniazid and rifapentine. Of 5,311 immigrant visa applicants recruited, 2,438 (46%) consented to participate; 2,276 had an IGRA processed, and 484 (21%) tested positive. Among 452 participants eligible for treatment, 304 (67%) initiated treatment, and 268 (88%) completed treatment. We

demonstrated that using the overseas medical examination to provide voluntary LTBI testing and treatment should be considered to advance US TB elimination efforts."

Statistics

	Total Cases	*Total Deaths*
Global	44,335,197	5,983,728
United States	79,197,392	956,293

JHU CSSE as of 1000 ET 04 March 2022

	Cases Cumulative Count	*Hospitalization Cumulative Count*	*Death Cumulative Count*
Virginia	1,645,791	47,509	18,955
Chesapeake	49,397	1,382	465
Hampton	27,362	736	310
Newport News	35,889	957	378
Norfolk	41,232	1,562	457
Portsmouth	20,613	1,044	308
Suffolk	18,531	769	286
Virginia Beach	88,545	3,652	780

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